ORIGINAL ARTICLE

Rev Bras Cir Cardiovasc 2008; 23(2): 216-223

Intracardiac correction of Tetralogy of Fallot in the first year of life. Short-term and midium-term results

Correção intracardíaca da tetralogia de Fallot no primeiro ano de vida. Resultados a curto e médio prazos

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RBCCV 44205-977

Abstract

Objective: **To evaluate short and medium term results of elective intracardiac correction of tetralogy of Fallot in the first year of life.**

Methods: **From January 1996 to October 2004, 67 consecutive infants ranging in age from 1 to 11 months (mean: 7.2 months) and weighing from 4 to 10 kigograms (mean: 7.1 kilograms) underwent elective total repair of tetralogy of Fallot. Intracardiac correction was accomplished with conventional cardiopulmonary bypass and moderate hypothermia. Intracardiac repair was accomplished through right ventriculotomy in 60 (89.5%) cases and by a transatrial-pulmonary approach in seven (10.5%).**

Results: **Bypass time ranged from 35 to 147 minutes (mean: 78.8 ± 21 minutes) and aorta cross clamp time ranged from 25 to 86 minutes (mean: 51.8 ± 15.6 minutes). A transannular right ventricular outflow patch was necessary in 50 (64.1%) patients. Right ventricle to pulmonary artery gradient after correction varied from 0 to 54 mmHg (mean:15.5 ± 10.8 mmHg). There were two (2,98%) early deaths. Follow-up of the 65 survivors ranged from 7 to 115 months (mean:44.0 ± 35 months). There was one late non-cardiac death. All other patients are asymptomatic. The actuarial probability of survival at 12 years, including operative mortality, was 97%. Ten patients were evaluated by cardiac magnetic angioresoanance imaging.**

Conclusions: **Intracardiac correction of tetralogy of Fallot in the first year of life may be performed with low morbidity and mortality and good late results.**

Descriptors: **Tetralogy of Fallot/surgery. Heart defects, congenital. Treatment outcome. Child. Follow-up studies.**

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Article received on January 23th, 2008
Article accepted on May 21th, 2008

Resumo

Objetivo: **Avaliar os resultados a curto e médio prazos da correção intracardíaca da tetralogia de Fallot no primeiro ano de vida.**

Métodos: **De janeiro de 1996 a outubro de 2004, 67 crianças com idade variando de 1 a 11 meses (média: 7,2 meses) e pesando entre 4 a 10 quilos (média: 7,1 kg) foram eletivamente submetidas a correção intracardíaca da tetralogia de Fallot. A cirurgia foi realizada com circulação extracorpórea convencional e hipotermia moderada. Ventriculotomia direita foi realizada em 60 (89,5%) casos e em sete (10,5%) utilizou-se a abordagem do defeito pela via atriopulmonar.**

Resultados: **O tempo de circulação extracorpórea variou de 35 a 147 minutos (média:78,8 ± 21 minutos), e o tempo de pinçamento da aorta variou de 25 a 86 minutos (média: 51,8 ± 15,6 minutos). Ampliação transanular da via de saída do ventrículo direito foi necessária em 50 (64,1%) casos. O gradiente entre o ventrículo direito e a artéria pulmonar, após a correção, variou de 0 a 54 mmHg (média: 15,5 ± 10,8 mmHg). Ocorreram dois (2,98%) óbitos no pós-operatório imediato. O seguimento tardio variou de 7 a 115 meses (média: 44,0 ± 35 meses). Houve uma morte tardia não-cardíaca. Todos os outros pacientes estão assintomáticos. A curva de sobrevida actuarial, incluindo a mortalidade operatória, revelou que a probabilidade de sobrevida, 12 anos após a operação, é de 97%. Dez pacientes foram avaliados por angiorresonância magnética nuclear.**

Conclusões: **A correção intracardíaca da tetralogia de Fallot no primeiro ano de vida pode ser feita com baixas morbidade e mortalidade e bons resultados tardios.**

Descritores: **Tetralogia de Fallot/cirurgia. Cardiopatias congênitas. Resultado de tratamento. Criança. Seguimentos.**

INTRODUCTION

In early attempts at correction of tetralogy of Fallot with cardiopulmonary bypass, there was a high mortality rate for young children. The result was that surgeons adopted the following two-stage surgical treatment: a shunt operation (preferably the Blalock – Taussig operation) within the first two or three years of life, and correction with cardiopulmonary bypass in older children [1]. In 1973, Barratt-Boyes and Neutze [2] and Starr et al. [3] independently proposed the definitive correction in the first year of life. The advantages and disadvantages of this treatment have been investigated over the years, with evidence that early correction reduces the side effects on vital organs (including the heart itself, which can suffer from hypoxemia) [4,5]. The early correction of tetralogy of Fallot has now been performed in several centers [6-19] with low mortality, but this is still a controversial aspect of the surgical treatment of this anomaly.

In the Heart Institute of Pernambuco (Real Hospital of the Beneficência Portuguesa, Pernambuco), a protocol was adopted in 1996 for performing intracardiac correction in all cases of classic tetralogy of Fallot fever in the first year of life (regardless of age and weight) [20,21]. The aim of this study is to evaluate the immediate morbidity and mortality and late results related to survival, the presence of symptoms, the need for reoperation and right ventricular function in the first 67 cases of tetralogy of Fallot operated in the first year of life in our Institution.

METHODS

Between January 1996 and October 2004, 67 children under one year of age electively underwent intracardiac correction of tetralogy of Fallot in the Heart Institute of Pernambuco (Real Hospital Português). Thirty-six (53.7%) patients were male and 31 (46.3%) were female. Age ranged from 1 to 11 months (mean: 7.2 months), and weight ranged from 4 to 10 kg (mean: 7.1 kg). This group of children represents all the cases of classic tetralogy of Fallot admitted to the Institution in the aforementioned period.

Diagnosis

In all of the patients, the medical history was obtained and a physical examination, chest radiography, electrocardiogram and Doppler echocardiography were performed. One child had undergone cardiac catheterization at another hospital.

Operative technique

All patients underwent surgery with the use of conventional cardiopulmonary bypass with membrane oxygenators and moderate hypothermia (25º). Myocardial protection was obtained by infusing cold crystalloid cardioplegic solution into the aorta at a dose of 350ml/m^2/SC (half of this dose was repeated every 20 minutes after the initial dose). Topical hypothermia of the heart was also obtained. The intracardiac correction was peformed using transventricular approach in 60 (89.5%) cases, and using atriopulmonary approach was used in seven (10.5%) cases. Surgeons decided on the type of approach after inspecting the right ventricle outflow tract and the pulmonary ring, but, in general, in the procedure's early stages, the preference was transverse ventriculotomy. Gradually, longitudinal ventriculotomy has become a more usual choice.

From the 60 patients who underwent surgery with the transventricular approach, the longitudinal incision was performed in 33 (55%) patients, and the transverse was performed in 27 (45%). However, in 14 (23.3%) of the 27 patients who underwent transverse ventriculotomy, there

was a need for enlargement of the right ventricle outflow tract and pulmonary ring after resection of the infundibulum. Thus, another small longitudinal ventriculotomy (a technique called double ventriculotomy) was performed.

Fifty (74.6%) patients underwent enlargement of the right ventricle outflow tract using a bovine pericardium graft. In 43 (64.1%) patients, this procedure was extended to the ring and the pulmonary artery trunk.

The atriopulmonary technique was used only in patients who had their important coronary arteries crossing the right ventricle outflow tract, which prevented a satisfactory ventriculotomy.

Trans-operative evaluation

We used pressure measurements of the right ventricle and the pulmonary artery taken after the infusion interruption in 59 (88%) cases. Blood samples were collected from the right atrium and ventricle to verify the presence of residual interventricular communication.

In each case, cardiopulmonary bypass time and aortic clamping were evaluated.

Immediate postoperative

In the recovery room, all children were maintained on ventilator assistance using a volume respirator until they were conscious enough and without hemodynamic instability or excessive bleeding.

To evaluate the immediate results, the following factors were analyzed:

a) Immediate mortality - defined as death within 30 days of the operation.

b) Cause of immediate death

c) Significant postoperative complications - defined as any complication that may risk the surgery's success.

Late postoperative

The information regarding late evolution was obtained in outpatient consultations in which the patients received clinical, electrocardiographic, radiological and echocardiographic exams. Ten (14.9%) patients underwent magnetic nuclear angioresonance. The magnetic nuclear angioresonance technique used consisted of: a) cine magnetic resonance of the heart (FISP technique) to evaluate volume, mass and right ventricular ejection fraction (Figure 1); b) quantification of pulmonary regurgitation through phase-contrast imaging; and c) Three-Dimensional Gadolinium-Enhanced Magnetic Resonance Angiography to evaluate central pulmonary arteries (Figure 2).

We considered the following late-evolution parameters:

a) Late mortality – in case of death, we worked to identify the cause;

b) Functional capacity – determined by the presence of symptoms;

c) The need for reoperation; and

d) Non-invasive hemodynamic evaluation of the right ventricle in 10 patients who underwent **angioresonance**. The following factors were evaluated: right ventricle ejection fraction (RVEF), right ventricular end-diastolic volume (RVEDV), right ventricular systolic volume (RVSV), right ventricular mass (RVM) and pulmonary regurgitation fraction (PRF). Additionally, the morphology of the pulmonary arteries was analyzed.

Fig.1 - Magnetic nuclear angioresonance showing the four chambers

Fig.2 - Magnetic nuclear angioresonance evaluating the pulmonary arteries and the right ventricle outflow tract

Statistical analysis

The categorical data were summarized by absolute and relative percentile frequencies, and the numerical data were summarized by average and median measures of location, as well as by dispersion (standard deviation, maximum and

minimum value). These numerical data were presented throughout the text to illustrate the description of the series of cases. The actuarial survival curve was constructed using the Kaplan-Meier method.

Ethical procedures

The protocol used in this study was approved by the Committee on Ethics in Research of the Heart Institute of Pernambuco.

RESULTS

Diagnosis

Fifty-eight (86.5%) children presented symptoms of hypoxemia and nine (13.5%) were acyanotic and asymptomatic. In all cases, the clinical, electrocardiographic and radiological findings suggested tetralogy of Fallot. The definitive diagnosis was established in all cases using two-dimensional Doppler echocardiography.

Transoperative data

The time of cardiopulmonary bypass ranged from 35 to 147 minutes (mean: 78.8 ± 21 min), and the time of aortic clamping ranged from 25 to 86 minutes (mean: 51.8 ± 15.6 min). In 50 (74%) patients, the right ventricle outflow tract was enlarged, and in 43 (64%) children, this procedure was transannular. The pressure gradient between the right ventricle and the pulmonary artery in the studied patients ranged from 0 to 54 mmHg (mean: 15.5 ± 10.8 mm Hg). No residual shunts were detected by gasometry.

Immediate postoperative

There were two (2.98%) deaths in the immediate postoperative period. The first patient was 4 months old, weighed 4 kgs and presented poor anatomy characterized by hypoplasia of the pulmonary ring and branches. There was extensive transannular enlargement of the right ventricle outflow tract. The infusion interruption was difficult to reach and the appropriate hemodynamic stability was reached only after high doses of inotropic drugs. The child continued to present low cardiac output and secondary renal failure, and peritoneal dialysis was performed. The death occurred on the day following the operation.

The second death occurred in a 7-month-old child, who weighed 7kg and presented with very favorable anatomy. The child received an infundibulectomy, and closure of the interventricular communication was performed using transverse ventriculomoty. In the immediate postoperative evolution, the patient presented sudden ventricular fibrillation without a clear cause. Return to sinus rhythm was slow, although measures of reanimation were quickly taken. As a result of this event, the child developed renal failure and underwent peritoneal dialysis. The patient died on the second postoperative day.

Among the 65 patients who survived the surgery and were discharged from hospital, the great majority presented postoperative evolution without complications. Six children presented the following non-fatal postoperative complications: 1) in one case, bleeding and cardiac tamponade that required reoperation; 2) in one case, cardiorespiratory arrest due to hyperpotassemia followed by bronchoaspiration and respiratory failure, which required intubation and assisted ventilation for five days; and 3) in four children, cardiac insufficiency that was difficult to control.

Late postoperative

Data relating to late postoperative evolution were obtained in all patients during clinical follow-ups that ranged from 7 to 115 months, with a mean of 44.0 ± 35 months (median = 36).

There was one death from meningitis in the seventh month of postoperative. All other patients presented excellent evolution and are asymptomatic. Only nine (13.8%) use medication.

No patient needed reoperation because there was excellent clinical evolution. In no cases the postoperative echocardiography evaluation showed significant or gradient residual interventricular communication above 40 mmHg along the right ventricle outflow tract.

The survival actuarial curve (calculated using the Kaplan-Meier method (Figure 3) included operative mortality and showed that the probability of survival at 12 years of surgery is 97%.

Kaplan-Meier Survival Probability Estimates are presented in Table 2. Figure 3 shows the survival curve. The dotted lines represent a confidence interval of 95% for this curve.

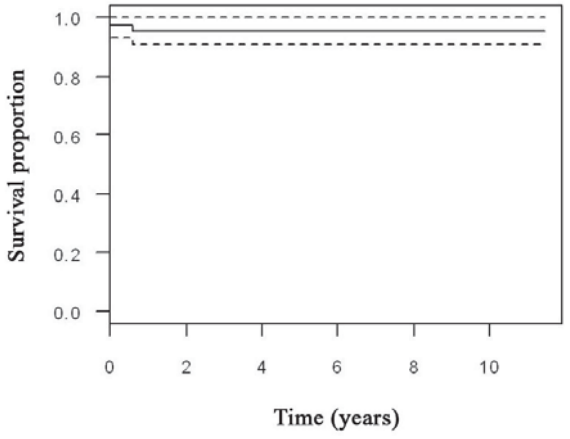

Fig.3 – Kaplan-Meier survival curve

Table 1. Kaplan-Meier Survival Probability Estimates

Time (days)	Number under risk	Number of failures	Survival probability	IC95% for the survival probability	
				Inferior limit	Superior limit
1	67	2	97.0%	92.9%	100%
212	65	1	95.5%	90.6%	100%

CI95%: 95% Confidence Interval

Table 2. Noninvasive hemodynamic data of the right ventricle using magnetic resonance.

Case	Gender	Age (years)	RVEF (%)	RVEDV (ml)	RVSV (ml)	RV mass (grams)	Pulmonary Regurgitation Fraction (PRF) (%)	Pulmonary arteries
8	M	9	49 (47-76)	108(50-88)	53(29-52)	37(18-32)	38(moderate)	Well-developed
9	M	9	37(47-76)	142(50-88)	52(29-52)	51(18-32)	Absent	Well-developed
10	M	9	48(47-76)	102(50-88)	48(29-52)	26(18-32)	18(slight)	Well-developed
17	F	10	52(47-76)	110(54-106)	57(32-62)	48(20-38)	14(slight)	Dilation RVSV/moderate stenosis in the PT and RBPA /severe stenosis in the LBPA
33	F	5	53(47-76)	85(32-52)	46(19-31)	26(12-19)	Absent	Slight stenosis in the PT and RBPA and moderate in the LBPA
41	F	5	39(47-76)	88(32-52)	44(19-31)	27(12-19)	42(severe)	Slight hypoplasia of the RBPA/RVOT Dilation
49	M	4	55 (47-76)	61(30-44)	34(18-26)	15(11-16)	43(severe)	LBPA Dilation
52	F	3	48(47-76)	34(26-38)	18(15-22)	15(9-14)	Absent	Well-developed
57	M	3	30(47-76)	71(26-38)	22(16-23)	21(10-14)	16(slight)	Subvalvar moderate stenosis
59	M	3	36(47-76)	48(26-38)	16(16-23)	15(10-14)	24(moderate)	Well-developed

The data of noninvasive hemodynamic evaluation of the right ventricle through magnetic resonance (which was performed on 10 patients) are shown in Table 1. The graph analyzes the right ventricular ejection fraction (RVEF), the right ventricular end-diastolic volume (RVEDV), the right ventricular systolic volume (RVSV), the right ventricular mass, the pulmonary regurgitation fraction (PRF) and the morphology of the right ventricle outflow tract and the trunk and branches of the pulmonary arteries. There were no cases of residual interventricular communication.

The right ventricular ejection fraction (normal value 47% to 76%) was reduced in four patients and was normal in the other six.

The normal values of end-diastolic and systolic volume and of the right ventricle mass vary according to gender and age, and are shown in the Table 1 and are presented in brackets below the values from each case.

The right ventricular end-diastolic volume was normal in only one patient, and was increased in the other nine.

The right ventricular systolic volume was normal in six patients and was increased in the other four.

The right ventricular mass, estimated in grams, was normal or almost normal in four patients and was increased in the others.

Pulmonary regurgitation was absent in three patients, slight in three, moderate in two and significant in two.

The morphological analysis of the trunk and branches of the pulmonary artery showed significant alteration in only one patient, who showed a severe stenosis in the left branch of the pulmonary artery, and who had already received a stent implantation.

The analysis of all hemodynamic data obtained in each case shows that there were no significant alteration in right ventricular function, which is supported by the excellent clinical evolution of the children.

DISCUSSION

The evidence from Barratt-Boyes and Neutze [2] and Starr et al. [3] in 1973, which proved that the tetralogy of Fallot could be corrected with cardiopulmonary bypass in the first year of life with low mortality rates, convinced several surgical groups to adopt the treatment [4-14]. At that time, it was already considered unlikely that late

results would be different from those obtained in older children [4].

The possible benefits of correction in the first year of life may include: 1) early normalization of flow and pressure in all cardiac chambers; 2) interruption of the hypertrophy process of the right ventricle that occurs when this cavity works with presence of pulmonary stenosis; 3) the possibility of a more narrow resection of the infundibulum, which may lead to a decrease in incidences of ventricular arrhythmias in the late postoperative period; 4) early normalization of the arterial oxygen saturation, avoiding the harmful effects of chronic hypoxemia in other organs; 5) a way to avoid potential complications of shunt operations, particularly the distortion of the pulmonary arteries and development of pulmonary hypertension; and 6) clear economic and psycho-social advantages.

Obviously, these attractive arguments need to be proven with better clinical experiments that show low immediate mortality and morbidity rates and good late results. Castaneda [22] reported that, between 1973 and 1993, 330 cases of tetralogy of Fallot were operated in the first year of life with 14 hospital deaths (4.2%) and three late deaths (0.9%). These excellent results have been reproduced by other authors [6-8, 19]. Our experience also showed good results: we had immediate mortality of only 2.9% as well as low morbidity rates. Obviously, the decision to correct the tetralogy of Fallot in the first year of life presupposes that the surgical group has significant experience with handling this malformation and can arrange for more appropriate conditions. Otherwise, it may be better to choose to correct tetralogy of Fallot in two-stage surgery [23].

One of the most troublesome and controversial aspects of the correction of tetralogy of Fallot in the first year of life is the increase in the need for transannular enlargement of the right ventricle outflow tract. Analyzing the survival of children with tetralogy of Fallot operated in the first 18 months of life, Vobecky et al. [24] analyzed the fact that primary early correction seems to protect neurological function and left ventricular function, and seems to produce fewer arrhythmias. However, there is an increase in the need for a transannular patch, which may compromise right ventricular function in the late postoperative period. Kirklin et al. [25] considered implanting a transannular patch to be a significant risk factor for children with a body surface area less than 0.48m^2. The analysis of several series of children operated during childhood shows a use of transannular patch variable of 30 to 70%. In our experience, this was used in 64% of cases. Indeed, the greater or lesser occurrence of transannular enlargement reflects not only the severity of the stenosis of the pulmonary ring of the operated cases, but also the surgeon's fear of significant residual stenosis. If annular stenosis were actually significant, then performing a Blalock operation will not avoid the enlargement of the ring during a subsequent definitive correction.

Castaneda et al. [5] have established that the only two risk factors of correcting tetrology of Fallot in the first year of life are acute hypoplasia of the pulmonary arteries and the anomalous origin of the anterior descending artery from the right coronary artery. Groh et al. [26] and Reddy et al. [19] argue that the surgery should not be disregarded based only on the size of the pulmonary arteries. Their research keeps this aspect open for discussion. In the event of either abnormalies of origin of the anterior descending artery or the presence of another important artery crossing the right ventricle outflow tract, it is possible to use the atriopulmonary correction technique, which was performed in some of our patients.

The late results of correction of tetralogy of Fallot in the first year of life have been analyzed under many different aspects and have proven to be excellent when compared to those seen in older children [27-32]. Van Arsdell et al. [33] reviewed 227 consecutive cases of tetralogy of Fallot, all of which were operated at the Hospital for Sick Children in Toronto, and they concluded that the best survival and physiological result was obtained in children who received the operation between 3 and 11 months.

The late clinical evolution of our patients is compatible with the data in the literature, as all of our cases are asymptomatic, and the great majority do not use any medication. However, this does not imply an absence of sequels or residual anatomical problems. About 10% of the patients who underwent a correction of tetralogy of Fallot require new intervention to correct the residual interventricular communication, a right ventricle aneurysm, a stenosis, or severe pulmonary insufficiency [28].

Echocardiograms have been the most common diagnostic method in these patients, but the transthoracic echocardiography has limitations and often fails to provide hemodynamic results or any significant anatomical information. The recent use of nuclear magnetic resonance to evaluate cardiac function is a valuable contribution to postoperative follow-ups of patients who underwent correction of congenital heart diseases, especially of tetralogy of Fallot [34].

These recent advances in the use of magnetic nuclear angioresonance have helped create better evaluations of pulmonary regurgitation and the right ventricle function, making ti easier to decie the appropriate period to perform elective pulmonary valve replacement, which should be performed before irreversible right ventricular dysfunction occurs [35].

The relationship between the type of repair on the right ventricle outflow tract and its function in the late postoperative period has been the subject of several studies [36-38]. This is particularly important in children operated

in the first year of life, due to the more frequent use of transannular patches in this group of patients. Residual pulmonary regurgitation is associated with right ventricle dilation, dysfunction of both ventricles, decreased tolerance of exercise and increased risk of arrhythmias [36-38]. Thus, the evaluation of the pulmonary regurgitation quantity is fundamentally important from a clinical perspective.

We have recently started to perform magnetic nuclear angioresonance in children operated on for tetralogy of Fallot in the first year of life, and we have already been able to study 10 patients. The method was very useful for right ventricle morphofunctional evaluations. It was possible to identify a case in which there were significant stenoses in the left branch of the pulmonary artery, and there had already been a stent implantation and a previous heart dilatation using a balloon. The analysis of all data obtained through angioresonance has concluded that no patient has significant changes in right ventricular function, although two patients presented moderate changes and two presented severe pulmonary regurgitation, which requires a more careful control of these four cases.

Based not only on data from literature, but mainly on our experiences reported herein, we believe that the operation of choice for patients with classic tetralogy of Fallot in the first year of life should be primary intracardiac correction.

CONCLUSIONS

1) The elective intracardiac correction of tetralogy of Fallot in the first year of life may be performed with low rates of morbidity and mortality.

2) The correction of tetralogy of Fallot in the first year of life quickly restores the normal physiology of the heart and circulation and arterial oxygen saturation.

3) The late results of intracardiac correction of tetralogy in the first year of life are excellent in terms of mortality and clinical evolution. There are no significant gradients in the right ventricle outflow tract, and function of the right ventricle is satisfactory.

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